

CLAIMS

We claim:

1. A targeting construct comprising:
 - (a) a first polynucleotide sequence homologous to at least a first portion of a GPRC5B-like gene, wherein the GPRC5B-like gene comprises SEQ ID NO:1;
 - (b) a second polynucleotide sequence homologous to at least a second portion of the GPRC5B-like gene; and
 - (c) a selectable marker.
2. A method of producing a targeting construct, the method comprising:
 - (a) providing a first polynucleotide sequence homologous to at least a first portion of a GPRC5B-like gene, wherein the GPRC5B-like gene comprises SEQ ID NO:1;
 - (b) providing a second polynucleotide sequence homologous to at least a second portion of the GPRC5B-like gene;
 - (c) providing a selectable marker; and
 - (d) inserting the first sequence, second sequence, and selectable marker into a vector, to produce the targeting construct.
3. A cell comprising a disruption in a GPRC5B-like gene, wherein the GPRC5B-like gene comprises SEQ ID NO:1.
4. The cell of claim 3, wherein the cell is a murine cell.
5. The cell of claim 4, wherein the murine cell is an embryonic stem cell.
6. A non-human transgenic animal comprising a disruption in a GPRC5B-like gene, wherein the GPRC5B-like gene comprises SEQ ID NO:1.
7. The non-human transgenic animal of claim 6, wherein the transgenic animal is a mouse.
8. A cell derived from the transgenic mouse of claim 7.
9. A method of producing a transgenic mouse comprising a disruption in a GPRC5B-like gene, the method comprising:
 - (a) introducing the targeting construct of claim 1 into a cell;
 - (b) introducing the cell into a blastocyst;

(c) implanting the resulting blastocyst into a pseudopregnant mouse, wherein said pseudopregnant mouse gives birth to a chimeric mouse; and

(d) breeding the chimeric mouse to produce the transgenic mouse.

10. A method of identifying an agent that modulates the expression or function of a GPRC5B-like gene, the method comprising:

- providing a non-human transgenic animal comprising a disruption in a GPRC5B-like gene, wherein the GPRC5B-like gene comprises SEQ ID NO:1;
- administering an agent to the non-human transgenic animal; and
- determining whether the expression or function of the disrupted GPRC5B-like gene in the non-human transgenic animal is modulated.

11. A method of identifying an agent that modulates the expression or function of a GPRC5B-like gene, the method comprising:

- providing a cell comprising a disruption in a GPRC5B-like gene;
- contacting the cell with the agent; and
- determining whether the expression or function of the GPRC5B-like gene is modulated.

12. The method of claim 11, wherein the cell is derived from the non-human transgenic animal of claim 6.

13. An agent identified by the method of claim 10 or claim 11.

14. A transgenic mouse comprising a disruption in a GPRC5B-like gene, wherein there is no significant expression of the GPRC5B-like gene in the transgenic mouse.

15. A transgenic mouse comprising a homozygous disruption in a GPRC5B-like gene, wherein the transgenic mouse exhibits abnormal pain threshold.

16. The transgenic mouse of claim 15, wherein the transgenic mouse exhibits an increased pain threshold.

17. The transgenic mouse of claim 16, wherein the increased pain threshold is characterized by an increased latency to lick a hindpaw in response to a hot plate in a hot plate test, relative to a wild-type mouse.

18. A cell derived from the transgenic mouse of claim 14.

19. A method of identifying an agent that ameliorates a phenotype associated with a disruption in a GPRC5B-like gene, the method comprising:

(a) administering an agent to a transgenic mouse comprising a disruption in a GPRC5B-like gene, wherein the GPRC5B-like gene comprises SEQ ID NO:1; and

(b) determining whether the agent has an affect on pain threshold.

20. An agent identified by the method of claim 19

21. A method of identifying an agent that has an affect on pain sensitivity, the method comprising:

(a) providing a mouse expressing a GPRC5B-like gene, wherein the GPRC5B-like gene comprises SEQ ID NO:1;

(b) contacting the cell with a putative agent; and

(c) determining whether the agent has an affect on pain sensitivity in the mouse.

22. A method of identifying an agent that inhibits the activity, expression, or function of a GPRC5B-like gene, the method comprising:

(a) providing a cell expressing a GPRC5B-like gene;

(b) contacting the cell with an putative agent; and

(c) determining whether the putative agent has an affect on activity, expression, or function of the GPRC5B-like gene, wherein the agent has an affect on pain threshold.

23. An agent identified by the method of claim 21 or claim 22.

24. A method of treating pain, the method comprising administering to a subject in need a therapeutically effective amount of an agent that inhibits the activity or function of a GPRC5B-like protein, wherein the GPRC5B-like protein comprises SEQ ID NO:2.

25. A method of screening for biologically active agents, the method comprising:

(a) combining a putative agent with a mammalian GPRC5B-like polypeptide; and

(b) detecting an effect of the agent on GPRC5B-like polypeptide activity; wherein detection of a decrease or an increase in GPRC5B-like polypeptide activity is indicative of a biologically active agent.

26. A method of screening for biologically active agents, the method comprising:

(a) combining a putative agent with an isolated cell comprising a nucleic acid encoding a mammalian GPRC5B-like gene or a GPRC5B-like promoter sequence operably linked to a reporter gene; and

(b) detecting an effect of the agent on GPRC5B-like activity;
wherein detection of a decrease or an increase in GPRC5B activity is indicative of a biologically active agent.

27. A method of screening for biologically active agents, the method comprising:

(a) combining a putative agent with a non-human transgenic model comprising an exogenous and stably transfected mammalian GPRC5B-like gene or GPRC5B-like promoter sequence operably linked to a reporter gene; and

(b) detecting an effect of the agent on GPRC5B-like function;
wherein detection of a decrease or an increase in GPRC5B function is indicative of a biologically active agent.

28. The method of claim 27, wherein the agent has an effect on pain threshold in the non-human transgenic model.

29. An agonist or antagonist of a GPRC5B-like protein encoded by SEQ ID NO:1.

30. Phenotypic data associated with a transgenic mouse comprising a disruption in a GPRC5B-like gene, wherein the phenotypic data is in an electronic database.